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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,710	06/27/2003	Michael D. Edge	GTC-42D	6943

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,710	EDGE ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/27/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Applicant's preliminary amendment requested the cancellation of claims 1-17 and the addition of a new claim which applicant has numbered 36. This application does not contain any claims 18-35. Therefore applicant's claim 36 has been renumbered according to Rule 126 as claim 18. An action on the merits follows.

Nucleic acid and/or Amino acid Sequences

Applicant's submission of the paper sequence listing and CRF on 2/13/04 has been entered. Applicant's amendment to the specification also submitted on 2/13/04 has also been entered. However, pages 23 and 39 of the specification contain sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821 (a)(1) and (a)(2). This application continues fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, the amino acid and nucleic acid sequences listed in pages 23 and 39 of the specification contains sequences which are not identified by SEQ ID NOS. Please note that compliance to 37 CFR 1.821-1.825 requires that the specification be amended to recite SEQ ID NOS. for each recitation of a sequence in the specification. Further, it is unclear whether these sequences are present in the paper copy and CRF of the sequence listing filed in this application. If the sequences are present in the paper and CRF listings, applicant may fully

comply with 37 CFR 1.821 by amending the specification to include the proper SEQ ID NOS. If the sequences are not present on the filed paper and CRF listings, then new paper and CRF sequence listings are required as set forth in the Notice to Comply.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/42329, 11/13/97, hereafter referred to as Copley et al., in view of U.S. Patent No. 5,959,171, 9/28/99, filed on 8/17/94, hereafter referred to as Hyttinen et al. The applicant claims a method of making a transgenic fusion protein comprising a first member and a second member wherein the second

member is carboxypeptidase B enzyme, comprising: providing a non-human transgenic mammal which includes a transgene which provides for the expression of biologically active fusion protein in the milk of the mammal and allowing the transgene is be expressed, wherein the fusion protein is produced at levels of at least about 0.1 mg/ml in the mammal's milk.

Copley et al. teaches vectors and nucleic acids encoding a fusion protein comprising a humanized anti-CEA antibody and human carboxypeptidase B which express biologically active carboxypeptidase B enzyme fusion proteins (Copley et al., pages 59-62, and page 75). Copley et al. further teaches making transgenic non-human animals capable of expressing the anti-CEA antibody fusion protein (Copley et al., page 17). Specifically, Copley et al. teaches the expression of the encoded fusion proteins in transgenic non-human mammals in which the nucleic acid encoding the fusion protein is operably linked to a mammary promoter to direct the expression of the protein in the mammal's milk (Copley et al., page 17, lines 1-14). Copley et al. further teaches the recovery of the protein from the milk of the transgenic mammals (Copley et al., page 17, lines 9-10).

Although Copley et al. provides the teachings and motivation for making transgenic mammals which secrete fusion protein comprising carboxypeptidase B in the milk and methods of recovering the fusion protein from the milk, Copley et al. differs from the instant invention by not providing specific guidance as to the expected level of fusion protein found in the milk of the non-human transgenic mammals. However, at the time of filing, expression of fusion proteins in the milk of transgenic mammals was well developed. For example, Hyttinen teaches that the general idea of making and using transgenic bioreactors for the production of large quantities of proteins, particularly human proteins, was suggested as early as 1986 and that numerous

examples of transgenic bioreactors exist in the art, citing references from 1991-1992 (Hyttinen et al., column 1). Hyttinen et al. further supplements Copley et al. by teaching that transgenic mammals comprising a nucleic acid encoding a beta-lactoglobulin-hEPO fusion protein under transcriptional control of a mammary specific promoter are capable of expressing the fusion protein at concentrations of 0.2-1 mg/ml in the transgenic milk (Hyttinen et al., column 10, lines 30-35). It is noted that hEPO is an enzyme.

Therefore, in view of the motivation provided by Copley et al. for making a transgenic mammal which expresses a fusion protein comprising carboxypeptidase in the mammal's milk, and in view of the teachings of Hyttinen et al. that fusion proteins can be expressed in the milk of transgenic mammals at concentrations of 0.2-1.0 mg/ml, it would have been *prima facie* obvious to the skilled artisan at the time of filing to make and use the transgenic mammals which secrete carboxypeptidase fusion proteins in the milk as described by Copley et al. to produce at least 0.1 mg/ml of the carboxypeptidase B enzyme fusion protein in the transgenic milk. Further, based on successful use of transgenic bioreactors in expressing large quantities of a variety of human proteins and enzyme containing fusion proteins as taught by Hyttinen et al., and the successful demonstration of the expression of 0.2-1.0 mg/ml of an enzyme fusion protein in transgenic milk by Hyttinen et al., the skilled artisan would have had a reasonable expectation of success in expressing at least 0.1 mg/ml of carboxypeptidase B enzyme fusion protein in the milk of a transgenic mammal using the transgenic mammals described by Copley et al.

No claims is allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

Application No.: 10/608,710

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: the sequences disclosed on pages 23 and 39 do not have SEQ ID NOS .

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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